REMARKS

Claims 10, 12-14, 16-20, 27-29, 31, 34-37, 39-44, 47-51 and 54-60 are pending after the present amendments. As amended, the claims relate to compositions and methods of preparing an agglomerate of potassium clavulanate crystals having a weight percentage of between 0 % and 10 % potassium clavulanate crystals in the needle form, wherein the agglomerate is precipitated from a solution obtained from contacting a potassium clavulanate crystal in a solvent or mixture of solvents with an anti-solvent under stirring. The amendments are supported at least in the specification at page 7, lines 24-27, and also at page 1, line 32 and page 4, lines 7-10 (describing potassium clavulanate as needle-shaped crystals). Thus, no new matter is added. Applicants respectfully request reconsideration and withdrawal of the rejections in view of the amended claims.

Claim Rejections under 35 U.S.C. § 112, first and second ¶s

The Office previously rejected the term "randomly ordered" as allegedly being indefinite. (Final Office Action mailed 6/25/04, page 2). The Office also indicated that the claims "while enabling for Potassium clavulanate, does not reasonably provide enablement for alkali metal clavulanates." (Final Office Action, page 5). The amended claims do not include the term "randomly ordered" and are now limited to potassium clavulanates, rendering these rejections moot. Applicants therefore respectfully request that these rejections be withdrawn.

Furthermore, the Office previously made two rejections under 35 U.S.C. § 112, first ¶, as allegedly failing to comply with the written description requirement. Regarding the term "Carr index" in claim 31, Applicants gratefully acknowledge the Examiner's indication that "[t]he proposed claim language for claim 31 would have resolved the matter." (Advisory Action, page 4). Regarding the removal of the previous limitation of "high water affinity," Applicants respectfully submit that this removal does not broaden the invention beyond what the specification teaches.

More particularly, the claims as amended relate to agglomerates of potassium clavulanate, which is a hygroscopic β-lactam compound. (See e.g., Specification at page 1, lines 18-20; and at page 3, lines 4-5 and 24-25). Because potassium clavulanate is a "β-lactam compound

of a high water affinity," the written description is met. Applicants therefore respectfully request that this rejection be withdrawn.

Claim Rejections under 35 U.S.C. § 102

The Office rejected claims 37, 40-42, 44 and 46-52 under 35 U.S.C. § 102(b), as allegedly being anticipated by U.S. patent 4,454,069, 6,417,352 or 5,288,861. Applicants respectfully request reconsideration and withdrawal of these rejections in view of the amended claims.

U.S. patent number 4,454,069 describes potassium clavulanates obtained using a "normal" precipitation procedure. More specifically, the potassium clavulanates were obtained by adding potassium ethyl hexanoate in isopropanol to a solution of t-butylamine salt of clavulanate acid acetone solvate dissolved in acetone. (See, '069 patent, Examples 3 and 4). The potassium clavulanates obtained may be well-defined needles or waisted plate (See, col. 5:36-39).

U.S. patent number 6,417,352 also describes potassium clavulanates obtained by "normal" precipitation procedures. In particular, the potassium clavulanates were obtained by adding a solution of potassium ethyl hexanoate in isopropanol to a solution clavulanic acid in isopropanol. (See e.g., '352 patent at col. 4:40-56). Although the '352 patent does not specify the form of potassium clavulanates prepared, normal precipitation procedures were used, and thus, would be expected to produce potassium clavulanates in needle form.

U.S. patent 5,288,861 describes potassium clavulanate rosettes obtained using a reverse precipitation method where the clavulanate solution is added to the precipitating diluent in contrast to the "normal" precipitation procedure described above. (See '861 patent at col. 4:18-24). For example, a filtrate comprising potassium clavulanate in aqueous methanol is added to isopropanol/acetone. (See, '861 patent at Example 1). In the Advisory Action, the Office indicated that "applicants present no reasoning why these would have to be rosettes" (Advisory Action mailed 9/7/04, page 4).

Applicants respectfully submit that the '861 patent specifically describes the invention as relating to "crystalline potassium clavulanate being in the form of crystalline rosettes each comprising a plurality of needle crystals radiating out from a common nucleation point." (See '861 patent at col. 1:52-68). The Figures also show potassium clavulanate in rosette form. Because potassium clavulanates in rosette form have been excluded, the '861 patent does not anticipate 37, 40-42, 44 and 46-52.

None of the references above describes a potassium clavulanate agglomerate precipitated from a solution obtained from contacting a potassium clavulanate crystal in a solvent or mixture or solvents with an anti-solvent under stirring. Furthermore, only the '352 patent describes further processing of potassium clavulanate crystals obtained using a sodium clavulanate intermediate, using conditions different from the claimed invention. For instance, Example 1 of the '352 patent teaches the recrystallization of potassium clavulanate by first converting the clavulanate to clavulanic acid, followed by addition of a potassium-2-ethylhexanoate in isopropanol. Because none of the references teach every element of the claimed invention, Applicants respectfully request that these rejections be withdrawn.

Furthermore, the Office also rejected claims 37, 39-44 and 46-52 under 35 U.S.C. § 102(b), as allegedly being anticipated by WO 97/33564. Applicants respectfully request reconsideration and withdrawal of these rejections in view of the amended claims.

WO 97/33564 describes auxiliary-free agglomerates containing a β-lactam antibiotic by forming a paste from the β-lactam antibiotic and a liquid; and subsequently kneading and extruding the paste. The β–lactam agglomerate may be mixed with a second pharmaceutically active agent such as potassium clavulanate in powder form. (See e.g., WO 97/33564 on page 9, lines 21-22; and page 11, lines 17-18). However, WO 97/33564 fails to teach a potassium clavulanate agglomerate precipitated from a solution obtained from contacting a potassium clavulanate crystal in a solvent or mixture or solvents with an anti-solvent under stirring. Thus, WO 97/33564 does not anticipate, and Applicants respectfully request that this rejection be withdrawn.

Further, the Office rejected claims 10, 12-14, 16-19, 27-29, 31-32, 37, 42-44 and 51-54 under 35 U.S.C. § 102(b), as allegedly being anticipated by WO 98/21212. The Office also indicated that "[t]he lifting of the requirement for being highly hygroscopic broadens the claims. (Office Action, page 9). Applicants must respectfully disagree.

As previously indicated, the amended claims specifically relate to agglomerates comprising potassium clavulanate, which is a hygroscopic β–lactam compound. Thus, the absence of the term "high water affinity" does not broaden the claims beyond what the specification teaches. Furthermore, WO 98/21212 teaches the preparation of potassium clavulanate from an amine clavulanate intermediate, without <u>further</u> processing of the potassium clavulanate crystals obtained. Thus, WO 98/21212 fails to anticipate and Applicants respectfully request that this rejection be withdrawn.

<u>New claims 55-60</u>

Applicants also submit that new claims 55-60 are free of prior art. None of the art the Office cited teaches a process comprising contacting a potassium clavulanate crystal in water or ethanol, and contacting the resulting solution with an anti-solvent under stirring to cause precipitation of an agglomerate comprising potassium clavulanate having a weight percentage of between 0 % and 10 % potassium clavulanate crystals in needle form, and with the proviso that the rosette-like crystalline form of potassium clavulanate is excluded. Furthermore, new claims 58-69 are dependent from claim 37, and thus contain all the limitations of claim 37. Thus, Applicants respectfully request allowance of new claims 55-60.

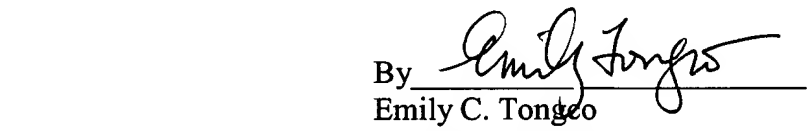
CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 246152015300. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: October 25, 2004

Respectfully submitted,

By 

Emily C. Tongeo
Registration No.: 46,473
MORRISON & FOERSTER LLP
3811 Valley Centre Drive, Suite 500
San Diego, California 92130
(858) 314-5413